DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

552291

FEB 25 2005

WARNING LETTER

VIA FEDERAL EXPRESS

Richard Meelia
CEO/President
Tyco Healthcare Group
15 Hamshire Street
Mansfield, MA 02048

Dear Richard Meelia:

During an inspection of your firm located in Juarez, Mexico on October 25, 2004, through October 28, 2004, our investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures a number of products including, but not limited to, SHILEY Tracheostomy Products, MON-A-THERM, WARMTOUCH and WARMFLO Temperature management products, and Mallinckrodt Tracheal Tubes. These products are devices under a United States law, the Federal Food, Drug, and Cosmetic Act (section 201(h) of the Act, (21 U.S.C. § 321(h)).

This inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act (21 U.S.C. § 351(h)), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820. Significant violations include, but are not limited to, the following:

1. Failure to establish and maintain procedures to adequately control environmental conditions, as required by 21 CFR 820.70(c). For example:

   a. The qualification/commissioning documentation that addresses the design, construction, placement, and installation for the controlled environment room ("white area") was not provided during our inspection. [redacted], specifies the "white area's" specifications to be [redacted] and [redacted]. Also, [redacted] establishes manufacturing parameters and operational conditions, e.g., limited personnel access, personnel gowning requirements, HVAC system with HEPA filtered air. However, no information was provided by your firm to substantiate how these

specifications, manufacturing parameters, and operational conditions were defined, appropriately qualified and some situations validated (i.e., HVAC system with HEPA filtration), and to establish appropriate environmental conditions to validate your firm's validated ethylene oxide (EtO) sterilization cycle.

b. Our Investigator observed employees who did not wear shoe covers and wore the same shoes as they wore outside the facility into the "white area." [redacted] does not require that employees working in the "white area" wear shoe covers. Your firm stated that [redacted] evaluated the effects of shoe covers on the environment in the clean room and on product bioburden and determined that eliminating the practice of wearing shoe covers appeared to have reduced the product's bioburden and recommended that this employee gowning practice be eliminated.

   Please explain the following concerns regarding the design of [redacted] (1) why were different products sampled for bioburden before and after removal of shoe covers; (2) please provide a justification for the environmental monitoring excursion observed during the study where the total microbial count limit was exceeded in [redacted] after shoe covers were eliminated; (3) please address seasonal variations in rainfall during the study period and its potential impact on airborne particulate counts; (4) please explain why the study protocol did not include approval signatures and was written 2 days after it was initiated; and (5) please explain why the sampling procedure did not include microbial monitoring of the floors. In contrast, the [redacted] provided in your firm's 11/17/04 response, [redacted], does require that employees use shoe covers in production areas. Please explain the discrepancy in the personnel shoe cover gowning practice between the [redacted] and the [redacted]

c. Environmental control systems have not been inspected periodically to verify that the system, including necessary equipment, is adequate and functioning properly. Specifically, your firm has not conducted filter integrity inspections of the HEPA filters in the controlled environment room since it was installed sometime in 1996. Procedures were not established or maintained to inspect the integrity or installation of the HEPA filters supplying air into the "white area."

d. Appropriate procedures were not followed for controlling environmental conditions. Specifically, our Investigator observed loss of power to the "white area" during the establishment inspection. During the power outage, your firm did not monitor the partial pressure differential and/or

air flow between the "white area" and the uncontrolled areas as described in procedure [redacted]. Further, your firm did not have an established procedure to control environmental conditions of the "white area" during power outages.

2. Failure to review and evaluate process changes and perform revalidation where appropriate, as required by 21 CFR 820.75(c).

For example, the controlled environment room's ("white area's") specifications and environmental monitoring and maintenance procedures specified in [redacted] were not adequately evaluated to determine what re-qualification activities were needed after production of the Shiley cuff-less tracheostomy tubes was transferred from your firm's [redacted] facility to the Juarez, Mexico facility. The [redacted] plant had developed written procedures for monitoring the controlled environment room as a result of the design transfer process validation study. This study established maintenance schedules and environmental monitoring procedures. However, the environmental monitoring and maintenance procedures established for the Shiley tracheostomy tubes at the previous Irvine facility were not re-validated by the process validation study [redacted] evaluated the equipment used in the manufacture of the Shiley cuff-less tracheostomy product and the need to qualify such equipment. This validation study did not identify the white area or its air handling/HEPA filter equipment as equipment requiring validation and did not include an evaluation to justify why re-qualification was not necessary.

3. Failure to establish and maintain procedures to investigate the cause of nonconformities relating to product, processes, and the quality system, as required by 21 CFR 820.100(a)(2).

For example, between [redacted] through [redacted] your firm took four corrective actions as a result of high microbial counts found in the controlled environment room but failed to investigate the root cause of the high counts. Also, during our review of 5 of your firm's 140 Quality Strategic Response (QSR) reports, the Investigator observed that your firm failed to investigate the root cause of high microbial counts noted during the monthly environmental monitoring program although corrective action was taken.

4. Failure to verify or validate the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(4).

For example, CAPA report, [redacted], indicated that your firm took corrective and preventive actions after production personnel failed to clear the production line prior to start of [redacted]; however,

the CAPA report does not document the steps taken to verify whether the preventive steps taken were effective in preventing future line clearance failures. The CAPA report did not document the corrective actions, preventive actions, or verification of preventive action taken in response to this CAPA event.

This letter is not intended to be an all-inclusive list of violations at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, Form FDA 483 (FDA 483), issued at the closeout of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to correct the violations and to bring your products into compliance.

If you fail to take prompt corrective action, FDA may take regulatory action without further notice to you. Given the serious nature of these violations of the Act, FDA may detain your products without physical examination upon entry into the United States under section 801(a) of the Act (21 USC 381(a)), until the violations described in this letter are corrected, because the products appear to be adulterated within the meaning of section 501(h) of the Act (21 USC 351(h)). In addition, United States federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of government contracts.

In order to remove your products from detention, you should provide a written response to this Warning Letter as described below and correct the violations described in this letter. We will notify you if your response is adequate, and we may need to re-inspect your facility to verify that the appropriate corrections have been made.

We received responses from David Olson, Vice President Regulatory Affairs, dated November 17, 2004, and December 16, 2004, concerning our investigator's observations noted on the FDA 483. We acknowledge receipt of the response from David Olson dated January 20, 2005. This response is currently under review and we will respond under separate cover. We have reviewed your responses dated November 17, 2004, and December 16, 2004, and have concluded that it is inadequate for the following reasons:

1. Although the "white area's" design, consisting of engineering diagrams, was provided in your firm's 11/17/04 response, qualification and validation of the design, construction, placement, and installation was not provided. Your firm's 12/16/04 response states that re-validation of the "white area" is being performed and is scheduled to be completed by 12/30/04. Please submit the re-validation results of the "white area" for our review.

2. Your firm's responses dated 11/17/04 and 12/16/04 claims that environmental excursions are not an issue as long as subsequent bioburden testing results are acceptable. However, environmental conditions, including microbial and particulate action levels, have to be within established levels

used to validate your firm's ethylene oxide (EtO) sterilization cycle. Accordingly, please provide a rationale as to how the [redacted] particulate specifications and operational conditions are within established levels used to validate your firm's sterilization cycle. This rationale should include an evaluation of the appropriateness of the microbial action levels to the sterilization cycle's established limits. Finally, please address your firm's corrective action practice of allowing corrections to be made for environmental excursions without requiring that an NCR or QSR report be created and entered into your firm's CAPA subsystem.

3. Your firm's responses dated 11/17/04 and 12/16/04 contains procedure [redacted] requires that materials be covered with plastic material for protection, that unprotected materials are placed on QC-Hold for "further evaluation," and the manufacturing areas and equipment be cleaned and documented. However, the procedure does not specify the evaluation that needs to be conducted on affected materials and devices nor does it require that an NCR report, or other CAPA report, be opened to investigate the situation. Please explain how [redacted] requires investigations and documentation of the cause of nonconformities and provide a revised procedure which establishes these requirements.

4. Your firm's responses dated 11/17/04 and 12/16/04 did not provide information describing the handling or disposition of the products in the "white area" with airborne particulate counts that exceeded the µm particulate count action limit of [redacted] during the observed power outage on 10/25/04. Although an NCR was opened as a result of the high particulate count, your firm did not explain the corrective actions taken and stated that no additional investigations would be taken on the affected devices and components. Please provide additional information on the power outage investigation, including the bioburden evaluation, the cause of the excursions, and the corrective measures taken to establish that the "white area's" manufacturing environment is under a state of control.

5. Your firm's responses dated 11/17/04 and 12/16/04 state that the process validation study, [redacted] is planned for completion by 12/30/04. However, [redacted] does not define what equipment constitutes a "critical process piece of equipment" that requires validation. It is not clear why the air handling/HEPA filter equipment of the "white area" is not considered critical process equipment that requires qualification. Accordingly, please describe how the critical process equipment is qualified in the "white area's" validation study and include a justification for equipment that is determined not to require re-qualification.

6. Please provide verification of retraining and the daily audit of line clearance procedure and form initiated by your firm to verify the effectiveness of the preventive steps taken for line clearance failures for our review.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter, of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include all documentation of the corrective action you have taken. If you plan to make any corrections in the future, include those plans with your response to this letter as well. If the documentation is not in English, please provide a translation to facilitate our review.

Your response should be sent to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Enforcement B, Orthopedics, Physical Medicine, and Anesthesiology Devices Branch (OPMAD), 2094 Gaither Road, Rockville, Maryland 20850 USA, to the attention of William MacFarland, Chief OPMAD.

If you need help in understanding the contents of this letter, please contact William MacFarland at the above address or at (240) 276-0120 or FAX (240) 276-0129.

Sincerely yours,

Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health